ANALYTICAL SCIENCES AUGUST 2000, VOL. 16

Protonation Constants of Some *N*-Substituted Amidoximes in a 50% Ethanol–Water Mixture (v/v)

Nedime DÜRÜST,* M. Abdülkadir AKAY, Yaşar DÜRÜST,* and Esma KILIÇ**†**

**Department of Chemistry, Faculty of Arts & Science, University of Kocaeli, Türkiye*
***Department of Chemistry, Faculty of Science, University of Ankara, Türkiye*

The stoichiometric protonation constants of some *N*-substituted amidoximes have been determined potentiometrically in a 50% ethanol–water mixture (v/v) at 25˚C and at constant ionic strength. A calculation was peformed using a PC software. The variation of the protonation constants of these compounds was interpreted on the basis of structural effects exposed by the substituents and main skeleton.

(Received August 25, 1999; Accepted April 14, 2000)

Amidoximes are compounds bearing both hydroximino and amino functionality at the same carbon atom, and are thus closely associated with amides, amidines and hydroxamic acids. These compounds are of great importance for the synthesis of various heterocycles. The complex formation capability of amidoximes makes use of the determination of Cu, Hg, Pb, and group 8, 9 and 10 metals. Among the coordination compounds, those with Mo and W central atoms are the most important. Amidoximes have found numerous technological applications, such as corrosion inhibition, stabilizing polymers and paper strengthening. Amidoxime functionalized polymeric coatings are being developed for chemical electronic microsensors. Another important application of amidoximes is uranium recovery from seawater. Amidoximes, especially those carrying arylsulfonyl and pyridyl groups, were reported to have shown significant biological activities, like hypoglycaemic, analgesics, pesticides, herbicides, and antihypertensic.[1]

To the best of our knowledge, there has been no report concerning the determination of the protonation constants of *N*-substituted amidoximes. Upon contiuning our studies on the determination of the protonation constants,[2,3] in this study we considered the protonation constants of some *N*-substituted amidoximes in 50% ethanol–water mixtures (v/v). Since these compounds sparingly dissolve in water, an ethanol–water mixture was used as a medium in titrations. The stoichiometric protonation constants were measured by a potentiometric titration method and calculations were carried out using PKAS computer software.[4]

The structures and protonation constant values of the compounds under investigation are given in Table 1.

Experimental

All of the compounds studied were synthesized as described previously[5,6] and checked chromatographically for purity. Stock solutions of these compunds were prepared in purified ethanol.[7] The standard amidoxime solutions were prepared in 50% aqueous ethanol. A 0.1 M perchloric acid solution was prepared in water and standardized by titration against primary standard sodium carbonate. Double-distilled deionized water was used throughout the experiments. Chemically pure sodium perchloride was used to maintain a constant ionic strength. Sodium chloride and sodium perchloride were purchased from Merck and used as received. An alkali solution containing 0.1 M $NaClO_4$ was prepared using NaOH (Merck) in 50% ethanol–water mixture and standardized potentiometrically against a perchloric acid solution using Gran's plot techniques, allowing a determination of the dissolved carbonate impurity.[8,9]

Potentiometric titrations were performed in a 80-mL glass vessel equipped with a combined pH electrode (Ingold), nitrogen inlet and outlet tubes, a magnetic stirrer and a titrant inlet. The electrode was modified by substituting its aqueous potassium chloride solution for a mixture of 0.01 M NaCl + 0.09 M $NaClO_4$ saturated with AgCl. An Orion Model 720A pH ionmeter was used to measure the cell e.m.f. (the uncertainity of e.m.f. measurements was ±0.1 mV). The temperature was maintained at 25.0 ± 0.1˚C.

The potentiometric cell was calibrated before each experiment to obtain pH (=log[H^+]) values for the titration medium.[10] The ion products (K_w = [H^+][OH^-]) were calculated at a constant ionic strength of 0.1 M with $NaClO_4$ in 50% aqueous ethanol solutions based on measurements of [OH^-] and pH in several series of experiments. The standardization of the combined pH electrode was also checked in the alkali range by the addition of excess NaOH. By assuming the E°_{cell} value determined in the acidic range to be reliable and the [OH^-] concentration of a base added in excess, we calculated the reproducible values of pK_w for the examined 50% aqueous ethanol solution.[12] The pK_w value calculated using the experimental data is 14.28. We are not aware of any pK_w value present in the literature, obtained under a condition similar to those applied to determine the protonation constants as presented in this article. On the other hand, a pK_w of 14.28 can be stated to be in accord with that of presented in Ref. 12.

Potentiometric titrations were carried out at constant temperature and in an inert atmosphere of nitrogen with CO_2-free standardized 0.1 M NaOH in a 50.0 mL solution containing 0.1 M $NaClO_4$ (i) 2.5×10^{-3} M $HClO_4$ (for cell calibration) and

† To whom correspondence should be addressed.
E-mail: ekilic@science.ankara.edu.tr

Table 1 Stoichiometric protonation constants of *N*-substituted amidoximes at 25.0±0.1˚C, in 50% ethanol-water mixture (v/v). (μ=0.1 M $NaClO_4$)

	N-Substituted amidoxime		Stoichiometric protonation constants[b]		
	R_1[a]	R_2[a]	log K_1	log K_2	Δlog K_3[c]
1	Me	H	10.66 (±0.08)	5.69 (±0.08)	4.97
2	Ph	H	11.42 (±0.09)	4.68 (±0.02)	6.74
3	*p*-tolyl	H	11.60 (±0.10)	4.65 (±0.09)	6.95
4	Ph	Me	11.84 (±0.10)	5.24 (±0.05)	6.60
5	Ph	*p*-tolyl	10.66 (±0.12)	3.36 (±0.03)	7.30
6	Me	Bz	11.53 (±0.10)	5.63 (±0.05)	5.90
7	Me	*n*-Pr	11.21 (±0.11)	5.75 (±0.09)	5.46
8	2-pyridyl	Me	11.20 (±0.10)	4.11 (±0.04)	7.09
9	2-pyridyl	Et	11.21 (±0.10)	4.08 (±0.01)	7.13
10	2-pyridyl	*n*-Pr	11.49 (±0.09)	4.10 (±0.04)	7.39
11	2-pyridyl	1-naphthyl	11.05 (±0.11)	2.55 (±0.08)	8.50
12	4-pyridyl	Me	11.67 (±0.09)	3.96 (±0.10)	7.71
13	4-pyridyl	Et	11.24 (±0.09)	3.79 (±0.01)	7.45
14	4-pyridyl	Ph	10.93 (±0.08)	2.87 (±0.04)	8.06
15	4-pyridyl	*p*-tolyl	11.19 (±0.08)	3.26 (±0.01)	7.93
16	3-pyridyl	*p*-tolyl	11.37 (±0.10)	2.94 (±0.01)	8.43

a. Me: methyl, Ph: phenyl, Et: ethyl, *n*-Pr: n-propyl, Bz: benzyl. b. The values in parentheses represent standard errors. c. $\Delta\log K = \log K_1 - \log K_2$.

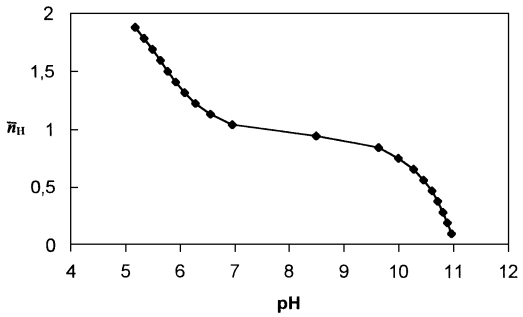
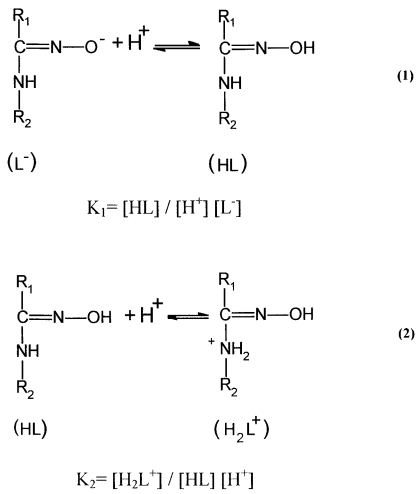


Fig. 1 The formation curve of *N*-methyl amidoxime in 50% ethanol–water mixture.



Scheme 1 *N*-Substituted amidoximes studied.

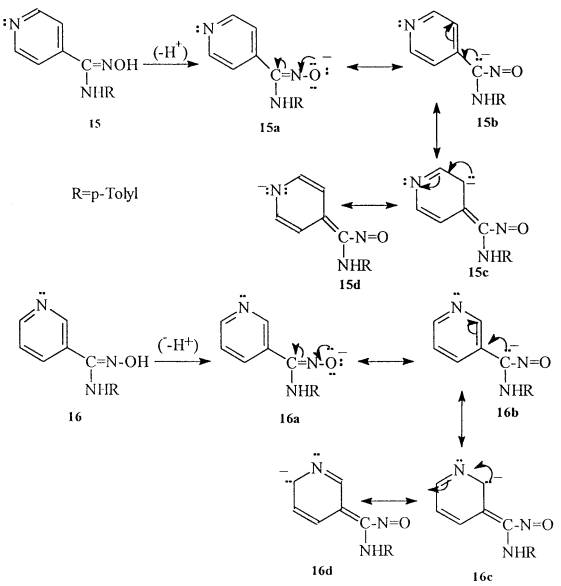
(ii) 2.5×10^{-3} M $HClO_4$ + 1.5×10^{-3} M amidoxime. The cell potential was read after waiting to establish the equilibrium throughout the titrations at a constant ionic strength of 0.1 M with $NaClO_4$. PKAS computer software was used to determine the protonation constants from potentiometric data.[4] The calculation procedure for the protonation constants related to the PKAS are given in Ref. 13.

Results and Discussion

Table 1 gives the stoichiometric protonation constants for *N*-substituted amidoximes studied in a 50% ethanol–water mixture (v/v) at 25˚C. These constants are described by Eqs. (1) and (2), where HL, L^- and H_2L^+ represent the *N*-substituted amidoxime, oximide anion and protonated amidoxime on amino nitrogen, respectively (Scheme 1). K_1 denotes the protonation equilibrium of the hydroxyimino group and K_2 corresponds to that of the *N*-substituted amino nitrogen. Also, the formation curves (n_H–pH) show rotational symmetry about the mid-point ($n_H = 1$, $\log H = -1/2 \log K_1K_2$), as described by Rossotti.[14] An example of the formation curve of *N*-methyl amidoxime obtained from the experimental data is given in Fig. 1.

Bordwell and co-workers[15-17] reported on the equilibrium acidities and bond-dissociation energies of some aldehyde and ketone oximes in non-aqueous media. According to Bordwell and Ji,[18] amidoximes are OH acids, not NH acids, since pK_a measurements of benzamidoxime and its *O*-methyl ester gave 23.0 and 26.0, respectively. The acidities of oximes stem from the C=NOH group and the lone pair of amino nitrogen causes a decrease in the OH acidity. Thus, we might expect changes in the acidity of this class of compounds when substitution occurs both at the azomethine carbon and the amino nitrogen. From the X-ray data of formamidoxime, the C=N and C–N bond distances were found to be 1.33 and 1.30 Å. Thus, the lone pair of the amino nitrogen can delocalize on the azomethine π system.[19]

From Table 1, log K_1 of benzamidoxime (**2**) is 11.42 and that of *p*-tolyl benzamidoxime (**3**) is 11.60. Substitution of *p*-tolyl instead of phenyl causes a 0.18 unit increase, which means a lowering of the acidity. This can be explained by electron release of the methyl group in *p*-tolyl. The smaller difference of log K_1 between benzamidoxime (**2**) and *p*-tolyl benzamidoxime (**3**) can probably be attributed to the fact that the methyl group is far from the OH group. No substantial difference was



Scheme 2 Reaction scheme.

observed in the log K_2 value of these two compounds. This result can be explained by the fact that substitution in the phenyl ring attached to the carbon atom does not affect the use of the lone pair on the amino nitrogen. However, substitution on the amino nitrogen by methyl and *p*-tolyl, as in entries **4** and **5**, causes substantial difference in both the log K_1 and log K_2 values. A 1.18 unit difference in log K_1 and 1.88 in log K_2, that is, the more acidic behavior of *N*-*p*-tolyl benzamidoxime (**5**) in comparison with *N*-methylbenzamidoxime (**4**), can be partially attributed to a delocalization of the negative charge through the phenyl ring on an amino nitrogen. Another explanation for this could be the bulkiness of *p*-tolyl, which may prevent the lone pair to be bonded to a proton.

In the case of acetamidoxime (**1**), *N*-*n*-propylacetamidoxime (**7**), and *N*-benzylacetamidoxime (**6**), the log K_1 values are found to be 10.66, 11.21 and 11.53, respectively. It can be seen that there is a relationship between alkyl substitution on the amino nitrogen and increasing log K_1 values. Again, the electron-releasing effect of the alkyl groups is the main factor in these examples.

When we compare amidoximes with 2-pyridyl substitution on azomethine carbon, entries (**8** – **11**), *n*-propylpyridine-2-carboxamidoxime (**10**) has a higher log K_1 value and *N*-1-naphthylpyridine-2-carboxamidoxime (**11**) has the lowest log K_1 value as well as also the lowest log K_2 value. The effective delocalization to the 10 π system of the naphthyl ring is strikingly lower both constants. A similar observation was reported for **14**, the π fluorene system.[20]

An examination of the stoichiometric protonation constant values, log K_1 and log K_2 of *N*-substituted pyridine-4-carboxamidoximes (**12** – **15**), clearly shows that alkyl substitution (*e.g.* methyl, ethyl) the enhances basicity and aromatic group substitution, especially the phenyl ring decreases log K_1. The methyl group on the phenyl in **15** causes an increase of log K_1 from 10.93 to 11.19.

In the case of 3-pyridyl substitution at the azomethine carbon, the log K_1 value of **16** is higher than that of **15**. The higher acidity of the compound **15** in comparison with **16** should be caused from the fact that resonance contributor **15d** gives an extra stability to the oximide anion generated by the dissociation of hydrogen, since the negative charge is accomodated on the more electronegative pyridine nitrogen, as depicted below (Scheme 2). Among the resonance structures of **16** (**16a** – **d**) there is no contributor to give extra stability to the anion.

We gratefully acknowledge the financial support of Ankara University Research Fund (Project No. 92-05-04-04) and Kocaeli University Research Fund.

References

1. D. N. Nicolaides and E. A. Varella, "*The Chemistry of Amidoximes in The Chemistry of Acid Derivatives*", ed. S. Patai, **1992**, Vol. 2, Suppl. B., John Wiley & Sons Ltd., 875.
2. E. Kılıç, F. Köseoğlu, and Ö. Başgut, *Anal. Chim. Acta*, **1994**, *294*, 215.
3. F. Köseoğlu, E. Kılıç, E. Canel, and N. Yılmaz, *Anal. Chim. Acta*, **1994**, *293*, 87.
4. A. E. Martell and R. J. Motekaitis, "*The Determination and Use of Stability Constants*", **1988**, VCH Publishers, Weinheim.
5. Y. Dürüst, H. Ağırbaş, and D. Sümengen, *Phosphorus, Sulfur, Silicon*, **1991**, *62*, 47.
6. H. Ağırbaş, D. Sümengen, Y. Dürüst, and N. Dürüst, *Synth. Commun*, **1992**, *22*, 209.
7. D. D. Perrin W. L. F. Armarego, "*Purification of Laboratory Chemicals*", **1992**, Pergamon, Oxford.
8. G. Gran, *Acta Chem. Scand.*, **1950**, *4*, 559.
9. G. Gran, *Analyst*, **1952**, *77*, 661.
10. T. Gündüz, E. Kılıç, F. Köseoğlu, and E. Canel, *Anal. Chim. Acta*, **1993**, *282*, 489.
11. E. P. Serjeant, "*Potentiometry and Potentiometric Titrations*", **1984**, Wiley, New York.
12. E. M. Woolley, D. G. Hurkot, L. G. Hepler, *J. Phys. Chem.*, **1970**, *74*, 3908.
13. R. J. Motekaitis and A. E. Martell, *Can. J. Chem.*, **1982**, *60*, 168.
14. H. Rossotti, "*The Study of Ionic Equilibria*", **1978**, Longmans, London.
15. F. G. Bordwell, Y. Zhao, and J. P. Cheng, *J. Phys. Org. Chem.*, **1998**, *11*, 10.
16. F. G. Bordwell and G. Z. Ji, *J. Am. Chem. Soc.*, **1991**, *113*, 8398.
17. F. G. Bordwell, D. L. Singer, and V. A. Satish, *J. Am. Chem. Soc.*, **1993**, *115*, 3543.
18. F. G. Bordwell and G. Z. Ji, *J. Org. Chem.*, **1992**, *57*, 3019.
19. A. Gieren, B. Dederer, L. Ugi, and S. Stuber, *Tetrahedron Lett.*, **1977**, 1507.
20. M. J. O'Donnell, W. D. Bennett, W. A. Bruder, W. N. Jacobsen, K. Knuth, B. LeClef, R. L. Polt, F. G. Bordwell, S. R. Mrozack, and T. A. Cripe, *J. Am. Chem. Soc.*, **1988**, *110*, 8520.